Risks of skin sensitization from contact with formaldehyde-releasing preservatives
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Formaldehyde-releasing preservatives as a class are preservatives found in art materials that are frequently related to allergic reactions in sensitized users. Assessments of the relationship between induction or elicitation of allergic responses are quantitatively related to the amount of preservative that comes into contact with the skin per unit area except when the skin contact area is <0.5 cm² where allergenic risk is related to the percentage of the allergen in the art material. A detailed discussion of this relationship is found in the accompanying paper, "Quantitative Risk Assessment of Skin Sensitizers and Irritants."

Formaldehyde-releasing preservatives are frequently used in cosmetics, skin care products and art materials. The potential for sensitization reactions is proportional to the amount of formaldehyde that may be released by a preservative. Among formaldehyde-releasing preservatives, amounts of formaldehyde that are released range from 0.3 to 10%. In North America, 2-4% of dermatitis patients are found to be sensitive to formaldehyde-releasing preservatives with rates in the EU being of the order of 2% (Jong et al, 2007).

The potential of contact with formaldehyde-releasing preservatives to induce a sensitization reaction has been investigated with human repeat insult patch testing (HRIPT), human maximization testing (HMT) and prophetic patch and use testing where sensitization reactions are monitored from use of cosmetics or skin-care products containing a formaldehyde-releasing preservative. As can be seen in the following table, as the level of releasable formaldehyde decreases, the risk of induction of sensitization decreases. There is, however, still a risk at the lowest level used in any trial, 200 ppm formaldehyde (equivalent to 20 mcg/cm²)

Human insult patch test results for formaldehyde-releasing preservatives*

<table>
<thead>
<tr>
<th># sensitized/# in trial</th>
<th>Releasable formaldehyde (ppm)</th>
<th>Releasable formaldehyde (mcg/cm²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8/415</td>
<td>1000</td>
<td>100</td>
</tr>
<tr>
<td>0/439</td>
<td>300</td>
<td>30</td>
</tr>
<tr>
<td>2/977</td>
<td>200</td>
<td>20</td>
</tr>
</tbody>
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*adapted from Cosmetic Ingredient Review (1986)
With HRIPT to formalin (a 37% aqueous solution of formaldehyde), Marzulli & Maibach (1974) found the NOEL for induction of sensitization to formaldehyde to be 37 mcg/cm$^2$ with none of 45 subjects being sensitized to this level. No irritation occurred with exposures to 0.25% formaldehyde.

When individuals previously sensitized to formaldehyde were patch tested against formaldehyde, Fischer et al (2011) found that the level of exposure necessary for elicitation of a reaction in 10% of the population they studied (called an ED$_{10}$) was found to be 20 mcg/cm$^2$. The EU's Executive Agency for Health and Consumers (2009) has recommended that formaldehyde levels in consumer products be limited to 0.02%.

Data for induction of sensitization to formaldehyde are limited to LOEL data sets. Dourson & Stara (1983) note that in such situations an uncertainty factor should be incorporated to approximate an NOEL data set. When the severity of the reaction is considered less than severe, an uncertainty factor of 3 is usually appropriate. In the case of formaldehyde-releasing preservatives, an acceptable exposure to formaldehyde to limit the risk of induction of an allergic response would be $200/3 = 67$ ppm. An exposure to 67 ppm formaldehyde is equivalent to an exposure to 6.7 mcg/cm$^2$. To address individual variation associated with application to the skin, an additional 10 fold uncertainty factor would be warranted; an acceptable exposure would be 0.7 mcg/cm$^2$. Exposure at this level would be 30 fold less than the ED$_{10}$ for elicitation of a reaction to formaldehyde in sensitized individuals and would be expected to be protective for individuals previously sensitized to formaldehyde as well.

References


